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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,344	09/20/1999	GERHARD SEEMANN	2481.1640	3847

5487 7590 06/24/2002

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EXAMINER	
SHUKLA, RAM R	
ART UNIT	PAPER NUMBER
1632	15

DATE MAILED: 06/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,344	SEEMANN ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Response filed 4-15-02 has been received and entered.

Election/Restrictions

Applicants elected p15-deoxyspergualin for prosecution in paper No 10. . Applicants elected osteoarthritis with respect to claims 7, 14, and 15 in Paper No. 10 is acknowledged.

2. Claims 1 and 4-15 are pending.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 4-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the tolerance of a mammal to transgenic cells, wherein the transgenic cells are produced in vivo after the administration of a vector carrying a transgene, by administering p15-deoxyspergualin to the mammal intravenously or intraperitoneally, before, during or after the administration of the vector, wherein said transgene encodes a protein, wherein a concomitant immunosuppressant therapy is discontinued, does not reasonably provide enablement for increasing tolerance in a mammal to transgenic cells produced in vitro or wherein the transgene of the transgenic cells produces a therapeutic protein that effects a treatment of a disease or wherein the transgenic cell produced in vivo after administration of a vector in vivo produce treatment of any disease for reasons of record set forth in the previous office action of 10-11-01. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 4-15-02 have been fully considered but they are not persuasive. Applicants first argue that in vitro methods for producing a transgenic cell are known to an artisan. Next, applicants quote Fed Reg 66(4):1105 in support of their argument that information well known in the art need not be described. In response, it is noted that the specification has to provide enablement for the invention claimed. Court states, "It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." (See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)).

It is noted that the specification does not provide any guidance as to how a transgenic cells and administer them to a mammal. It is reiterated that these routes of administration are not routine in the art. Furthermore, applicants do not provide any guidance as to what doses of the cell would be used by these routes of administration and as to how the pharmaceutical p15-deoxyspergualin would be administered to a mammal in which the transgenic cells would have been

administered by the routes recites. Next, applicants argue that the examiner has not provided scientific basis for the assertions. In response it is noted that administration of transgenic cells intranasaly, topically, percutaneously, by inhalation or by other 15-16 routes of administration recited was not routine in the art at the time of the invention and therefore, an artisan have to plan and practice the claimed invention of administration and such would require extensive experimentation. If applicants argue that the methods were routine at the time of invention, they are advised to provide evidence that such methods were routine at the time of the invention. It is noted that applicants have not provided any evidence that such methods were routine. Applicants argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979).

Next applicants argue that the examiner has questioned the integrity of data. These arguments are misplaced, because the office action had tried to interpret data in light of the disclosure in the specification and the PNAS paper. It is noted that the specification does not disclose the structure of the recombinant adenoviral vector used in the examples of the specification. Rather it cites the PNAS paper for the recombinant adenovirus used in the experiment (see lines 35-39 of page 8 of the specification). Since, the cited paper teaches multiple vectors, it is not clear as to how would an artisan know which of the vectors was used in the example disclosed in the specification. Even in the arguments, applicants did not identify the particular vector used in the specification. Applicants argue that it was made clear at pages 9-10 of the instant application that identical vector was administered to both immunosuppressed mice and control mice. While this is not contested, applicants fail to take into account role of different genes of adenovirus in producing immune response in an animal and unless an artisan knows the nature and structure of the adenovirus used in the specification, would not be able to understand the extent of protection by DSG. It is reiterated that arguments alone cannot take place of evidence lacking in the record.

Next, applicants have characterized all the reviews and issues of enablement raised in the previous office action as erroneous. It is noted that the previous office action raised following specific issues based on the state of the art of gene therapy

and in view of the review articles: role of transgene in immune response against an adenoviral vector, role of different genes of adenovirus in producing an immune response, and state of gene therapy, unpredictability of cell transplantation etc. The applicants did not provide any evidence as to how the issues raised in the office action were erroneous nor did they provide any specific data or guidance to support their contention that the specification was enabling in view of the unpredictability of the art of gene therapy and immune response generated by adenoviral vectors. Applicants have provided a list of patents in support of their argument (but no evidence) that gene therapy and transplantation etc. Applicants argue that since patent office issued over 87 patents that contain the phrase "gene therapy" in their title. However, applicants fail to provide any evidence that these patents enabled every method of gene therapy. Additionally, a title of a patent is not an indication of what is enabled by the disclosure of the patent. Therefore, applicants have failed to provide any evidence to support their arguments that the specification was enabling for the broad scope of the invention claimed and the scope of rejection as set forth in the previous office action is maintained for reasons of record set forth in the previous office action of 10-11-01 and as discussed above.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 4-15 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record set forth in the previous office action of 10-11-01.

Applicants failed to address the grounds of rejection set forth in the previous office action.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> > (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 4, 9, 10, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Smith et al (Gene Therapy 3:496-502, 1996; abstract only) for reasons of record set forth in the previous office action of 10-11-01.

9. Claims 1, 4, 9, 10, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Trapnell et al (WO 96/12406, 05-02-1996) for reasons of record set forth in the previous office action of 10-11-01.

10.

Response to Arguments

Applicant's arguments filed 4-15-02 have been fully considered but they are not persuasive. Applicants have argued that the applicants measured gene product, not the amount of adenovirus. However, these arguments are not persuasive because none of the claims have such a limitation. Further, applicants argue that applicants teach tolerance to a transgenic cell and none of the cited arts teaches. In response, it is noted that the in vitro produced transgenic cells and their administration is not enabled as discussed above and the in vivo cells are the cells of the mammal itself. Therefore, any immune response produced would be due to a gene product or the foreign vector and therefore, the issue of immune tolerance against transgenic cell is not an issue.

11. No claim is allowed.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to **§** 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.

RAM R. SHUKLA, PH.D
PATENT EXAMINER